

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

Spyre Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

46-4312787

(I.R.S. Employer Identification Number)

221 Crescent Street

Building 23, Suite 105

Waltham, MA 02453

(617) 651-5940

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Heidy King-Jones

Chief Legal Officer and Corporate Secretary

Spyre Therapeutics, Inc.

221 Crescent Street

Building 23, Suite 105

Waltham, MA 02453

(617) 651-5940

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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San Francisco, CA 94111

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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any jurisdiction where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 20, 2024

PROSPECTUS



46,330,799 SHARES OF COMMON STOCK

This prospectus relates to the proposed resale or other disposition by the selling stockholders identified herein (the "Selling Stockholders") of up to (i) 31,137,912 shares of our common stock, par value \$0.0001 per share ("Common Stock"), (ii) 13,841,800 shares of Common Stock issuable upon the conversion of 346,045 shares of our Series A Non-Voting Convertible Preferred Stock, par value \$0.0001 per share (the "Series A Preferred Stock"), (iii) 666,680 shares of Common Stock issuable upon the conversion of 16,667 shares of Series B Non-Voting Convertible Preferred Stock, par value \$0.0001 (the "Series B Preferred Stock"), and (iv) 684,407 shares of Common Stock issuable upon the exercise of 684,407 warrants (the "Parapyre Warrants"). Subject to certain beneficial ownership limitations set by the preferred stockholder, each share of Series A Preferred Stock and Series B Preferred Stock is convertible into an aggregate of 40 shares of Common Stock. The shares of Common Stock registered by this prospectus are referred to herein as the "Resale Shares."

The Resale Shares, and the Series A Preferred Stock, the Series B Preferred Stock and the Parapyre Warrants from which such Resales Sales are convertible or exercisable, as applicable, were collectively issued and sold (i) to stockholders of Pre-Merger Spyre (as defined below) in connection with the Asset Acquisition (as defined below), which closed on June 22, 2023, (ii) to certain accredited investors in a private placement (the "June 2023 PIPE" and, together with the Asset Acquisition, the "June 2023 Transactions"), which closed on June 26, 2023, (iii) to certain accredited investors in a private placement (the "December 2023 PIPE"), which closed on December 11, 2023, (iv) to certain accredited investors in a private placement (the "March 2024 PIPE"), which closed on March 20, 2024, (v) to a certain accredited investor in exchange for shares of Series A Preferred Stock (the "April 2024 Exchange"), which closed on April 25, 2024, and (vi) to Parapyre Holding LLC ("Parapyre") on December 29, 2023 pursuant to the antibody discovery and option agreement, dated May 25, 2023, and subsequently amended and restated on September 29, 2023 and May 14, 2024, by and among us, Paragon Therapeutics, Inc. ("Paragon") and Parapyre (the "Paragon Agreement"). We are not selling any Resale Shares under this prospectus and will not receive any of the proceeds from the sale or other disposition of Resale Shares by the Selling Stockholders.

The Selling Stockholders may sell the Resale Shares on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, on the over-the-counter market, in one or more transactions otherwise than on these exchanges or systems, such as privately negotiated transactions, or using a combination of these methods, and at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. See the disclosure under the heading "Plan of Distribution" elsewhere in this prospectus for more information about how the Selling Stockholders may sell or otherwise dispose of their Resale Shares hereunder.

The Selling Stockholders may sell any, all or none of the securities offered by this prospectus and we do not know when or in what amount the Selling Stockholders may sell their Resale Shares hereunder following the effective date of the registration statement of which this prospectus forms a part.

You should carefully read this prospectus and any applicable prospectus supplement before you invest in any of the securities being offered.

Our Common Stock is traded on the Nasdaq Global Select Market under the symbol "SYRE." The last reported sale price of our Common Stock on the Nasdaq Global Select Market, on September 19, 2024, was \$30.40 per share. We recommend that you obtain current market quotations for our Common Stock prior to making an investment decision.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "[Risk Factors](#)" contained in this prospectus beginning on page 4 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Prospectus dated , 2024

Table of Contents

	Page
<u>ABOUT THIS PROSPECTUS</u>	<u>i</u>
<u>CAUTIONARY STATEMENT CONCERNING FORWARD LOOKING STATEMENTS</u>	<u>ii</u>
<u>PROSPECTUS SUMMARY</u>	<u>1</u>
<u>THE OFFERING</u>	<u>2</u>
<u>RISK FACTORS</u>	<u>4</u>
<u>USE OF PROCEEDS</u>	<u>5</u>
<u>SELLING STOCKHOLDERS</u>	<u>6</u>
<u>PLAN OF DISTRIBUTION</u>	<u>14</u>
<u>LEGAL MATTERS</u>	<u>17</u>
<u>EXPERTS</u>	<u>17</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>17</u>
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	<u>18</u>

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC” or the “Commission”) utilizing a “shelf” registration process. Under this shelf registration process, the Selling Stockholders may, from time to time, sell the securities described in this prospectus in one or more offerings. Information about the Selling Stockholders may change over time.

This prospectus provides you with a general description of the Resale Shares the Selling Stockholders may offer. Each time the Selling Stockholder sells Resale Shares using this prospectus, to the extent necessary and required by law, we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the number of Resale Shares being offered, the manner of distribution, the identity of any underwriters or other counterparties and other specific terms related to the offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement made in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read this prospectus, any applicable prospectus supplement and the information incorporated by reference in this prospectus before making an investment in shares of our Common Stock. See “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” for more information.

This prospectus contains and incorporates by reference information that you should consider when making your investment decision. Neither we, nor the Selling Stockholders, have authorized anyone to give any information or to make any representation other than those contained in this prospectus. The Selling Stockholders are offering to sell, and seeking offers to buy, our securities only in jurisdictions where it is lawful to do so. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in any accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

In this prospectus, unless the context otherwise requires, the terms “Spyre,” “Aeglea BioTherapeutics, Inc.,” the “Company,” “we,” “us,” and “our” refer to Spyre Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

“Spyre” and all product candidate names are our common law trademarks. This prospectus contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

All references to “our product candidates,” “our programs” and “our pipeline” in this prospectus refer to the research programs with respect to which we have signed a license agreement for, exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights to pursuant to the Paragon Agreement.

Please be advised that on September 8, 2023, we effected a reverse stock split of our Common Stock at a ratio of 1-for-25 (the “Reverse Split”). Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this prospectus have been adjusted on a post-Reverse Split basis. In addition, on November 28, 2023, we changed our name from “Aeglea BioTherapeutics, Inc.” to “Spyre Therapeutics, Inc.”

CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These forward-looking statements involve a number of risks and uncertainties. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events.

All statements, other than statements of historical facts contained in this prospectus, including, without limitation, statements regarding: any future payouts under our contingent value rights issued in connection with the acquisition of Spyre Therapeutics, Inc. (“Pre-Merger Spyre”) (the “Asset Acquisition”); our ability to achieve the expected benefits or opportunities and related timing with respect to the Asset Acquisition or to monetize our legacy assets, our future results of operations and financial position, our business strategy, the length of time that we believe our existing cash resources will fund operations, our market size, our potential growth opportunities, our nonclinical and clinical development activities, the efficacy and safety profile of our product candidates, the potential therapeutic benefits and economic value of our product candidates, the timing and results of nonclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China on our operations, and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates. Forward-looking statements generally relate to future events or our future financial or operating performance. The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “predict,” “target,” “intend,” “could,” “would,” “should,” “project,” “plan,” “expect,” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Factors that might cause such a difference include the risks set forth under the caption “Risk Factors” in this prospectus and in the documents incorporated by reference in this prospectus. You should evaluate all forward-looking statements made in this prospectus in the context of these risks and uncertainties. We caution you that the risks, uncertainties and other factors referred to in this prospectus may not contain all of the risks, uncertainties and other factors that may affect our future results and operations.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus. While we believe that such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements. This prospectus and registration statement also contain or incorporate by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained such industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events

or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events, except as may be required under applicable U.S. securities laws. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our Common Stock. You should read the entire prospectus carefully, including “Risk Factors,” and the consolidated financial statements and related notes and information incorporated by reference into this prospectus, before making an investment decision. Some of the statements in this summary constitute forward-looking statements, see “Cautionary Statement Concerning Forward-Looking Statements.”

Our Company

We are a clinical stage biopharmaceutical company focused on developing next generation therapeutics for patients living with inflammatory bowel disease. We are advancing a pipeline of monoclonal antibodies, and combinations thereof, for the treatment of inflammatory bowel disease, including ulcerative colitis and Crohn’s disease, and plan to develop patient selection approaches for each of our programs.

For more information about our business, please see our most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed or will file with the SEC, and in other documents which are incorporated by reference into this prospectus.

Corporate Information

We were formed as a Limited Liability Company (“LLC”) in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and were converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On June 22, 2023, we completed the Asset Acquisition and on November 27, 2023, we completed our corporate rebranding, changing our name to Spyre Therapeutics, Inc.

Our principal executive offices are located at 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453 and our telephone number is (617) 651-5940. Our website is www.spyre.com. The information on, or that can be accessed through, our website is not part of this prospectus and is not incorporated by reference herein. We have included our website address in this prospectus solely as an inactive textual reference.

THE OFFERING

We are registering for resale by the Selling Stockholders named herein 46,330,799 shares as described below:

Shares offered by the Selling Stockholders	Up to (i) 31,137,912 shares of Common Stock, (ii) 13,841,800 shares of Common Stock issuable upon the conversion of 346,045 shares of Series A Preferred Stock, (iii) 666,680 shares of Common Stock issuable upon the conversion of 16,667 shares of Series B Preferred Stock and (iv) 684,407 shares of Common Stock issuable upon the exercise of 684,407 Parapyre Warrants.
Terms of the offering	The Selling Stockholders will determine when and how they will dispose of the Resale Shares.
Securities outstanding	As of June 30, 2024, there were 50,783,384 shares of our Common Stock, 346,045 shares of Series A Preferred Stock, 16,667 shares of Series B Preferred Stock and 684,407 Parapyre Warrants outstanding.
Use of proceeds	We will not receive any of the proceeds from the sale or other disposition of the Resale Shares by the Selling Stockholders. See “Use of Proceeds” on page 5 of this prospectus.
Risk factors	You should read and consider the information set forth under the heading “Risk Factors” in this prospectus, together with the risk factors and cautionary statements described in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, before deciding to invest in shares of our Common Stock.
Nasdaq Global Select Market Symbol	“SYRE”

Except as otherwise noted, the number of issued and outstanding shares of Common Stock does not include the following, as of June 30, 2024:

- 13,841,800 shares of Common Stock issuable upon the conversion of 346,045 shares of Series A Preferred Stock;
- 666,680 shares of Common Stock issuable upon the conversion of 16,667 shares of Series B Preferred Stock;
- 8,712,870 shares of Common Stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$15.43 per share;
- 153,865 shares of Common Stock issuable upon the vesting of restricted stock units outstanding;
- 4,311,298 shares of Common Stock reserved for issuance pursuant to future equity awards under our 2016 Equity Incentive Plan (the “2016 Plan”), as well as any future increases in the number of shares of Common Stock reserved for future issuance under the 2016 Plan;
- 191,794 shares of Common Stock reserved for issuance pursuant to future equity awards under our 2018 Equity Inducement Plan (the “2018 Plan”), as well as any future increases in the number of shares of Common Stock reserved for future issuance under the 2018 Plan;
- 430,645 shares of Common Stock reserved for future issuance under our 2016 Employee Stock Purchase Plan (the “2016 ESPP”), as well as any future increases in the number of shares of Common Stock reserved for future issuance under the 2016 ESPP; and

- 684,407 shares of Common Stock issuable upon the exercise of outstanding warrants having an exercise price of \$21.52 per share.

As of June 30, 2024, 740,296 shares of Series A Preferred Stock and 254,958 shares of Series B Preferred Stock have been converted to or exchanged for common stock and 346,045 shares of Series A Preferred Stock and 16,667 shares of Series B Preferred Stock were issued and outstanding.

Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this prospectus have been adjusted on a post-Reverse Split basis.

Unless otherwise indicated, all information in this prospectus assumes no exercise of outstanding stock options and warrants or vesting of restricted stock units as of June 30, 2024.

RISK FACTORS

Investing in our securities involves risks. You should carefully consider the risks, uncertainties and other factors described in our most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed or will file with the SEC, and in other documents which are incorporated by reference into this prospectus, as well as the risk factors and other information contained in or incorporated by reference into any accompanying prospectus supplement before investing in any of our securities. Our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected by any of these risks. The risks and uncertainties described in the documents incorporated by reference herein are not the only risks and uncertainties that you may face.

For more information about our SEC filings, please see “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

USE OF PROCEEDS

We are not selling any securities under this prospectus and we will not receive any proceeds from the sale of the Resale Shares covered hereby. The net proceeds from the sale of the Resale Shares offered by this prospectus will be received by the Selling Stockholders.

Subject to limited exceptions, the Selling Stockholders will pay any underwriting discounts and commissions and expenses incurred by the Selling Stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the Selling Stockholders in disposing of any of the Resale Shares. We will bear the costs, fees and expenses incurred in effecting the registration of the Resale Shares covered by this prospectus, including all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our independent registered public accounting firm.

SELLING STOCKHOLDERS

This prospectus covers the resale or other disposition from time to time by the Selling Stockholders identified in the table below of up to an aggregate of 46,330,799 shares of our Common Stock. The Selling Stockholders may from time to time offer and sell any or all of the Resale Shares set forth below pursuant to this prospectus and any accompanying prospectus supplement.

On June 22, 2023, we entered into a share purchase agreement (the “June 2023 SPA”), pursuant to which we sold an aggregate of 721,452 shares of our Series A Preferred Stock, each of which automatically converted into 40 shares of Common Stock, subject to certain beneficial ownership limitations set by each holder, pursuant to our Certificate of Designation of Series A Non-Voting Convertible Preferred Stock (the “Series A Certificate of Designation”), at an aggregate purchase price of approximately \$210 million. Also on June 22, 2023, we completed our acquisition of Pre-Merger Spyre in accordance with that certain Agreement and Plan of Merger (the “Acquisition Agreement”), dated June 22, 2023, by and among us, Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company, Sequoia Merger Sub II, LLC, a Delaware limited liability company and one of our wholly owned subsidiaries, and Pre-Merger Spyre, pursuant to which we issued an aggregate of 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock to certain of the Selling Stockholders.

On December 7, 2023, we entered into a share purchase agreement (the “December 2023 SPA”), pursuant to which we sold an aggregate of 6,000,000 shares of our Common Stock and 150,000 shares of our Series B Preferred Stock, each of which automatically converted into 40 shares of Common Stock, subject to certain beneficial ownership limitations set by each holder, pursuant to the Certificate of Designation of Series B Non-Voting Convertible Preferred Stock (the “Series B Certificate of Designation”), at an aggregate purchase price of \$180 million.

On December 29, 2023, we issued warrants to purchase 684,407 shares of Common Stock at an exercise price of \$21.52 per share, which was the closing price of a share of Common Stock on December 29, 2023, to Parapyre in accordance with the Paragon Agreement.

On March 18, 2024, we entered into a share purchase agreement (the “March 2024 SPA”), pursuant to which we sold an aggregate of 121,625 shares of our Series B Preferred Stock, each of which automatically converted into 40 shares of Common Stock, subject to certain beneficial ownership limitations set by each holder, pursuant to the Series B Certificate of Designation, at an aggregate purchase price of approximately \$180 million.

On April 23, 2024, we entered into an exchange agreement (the “April 2024 Exchange Agreement”) with a Selling Stockholder, pursuant to which such Selling Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of Common Stock.

This prospectus covers the resale or other disposition by the Selling Stockholders or their pledgees, donees, transferees or other successors-in-interest that receive their shares after the date of this prospectus of up to the total number of shares of Common Stock, shares of Common Stock issuable upon the conversion of the Series A Preferred Stock, shares of Common Stock issuable upon the conversion of the Series B Preferred Stock and shares of Common Stock issuable upon the exercise of the Parapyre Warrants issued to the Selling Stockholders pursuant to the Acquisition Agreement, the June 2023 SPA, the December 2023 SPA, the March 2024 SPA, the April 2024 Exchange and the Paragon Agreement, as applicable, that remain unsold by such Selling Stockholders.

We are registering the resale of the Resale Shares to permit the Selling Stockholders and their pledgees, donees, transferees or other successors-in interest that receive their shares after the date of this prospectus to resell or otherwise dispose of the shares in the manner contemplated under “Plan of Distribution” herein.

Except as otherwise disclosed herein, the Selling Stockholders do not have, and within the past three years have not had, any position, office or other material relationship with us.

The following table sets forth the names of the Selling Stockholders, the number of shares of our Common Stock beneficially owned by the Selling Stockholders, the number of shares of our Common Stock that may be

offered under this prospectus and the number of shares of our Common Stock that will be owned after this offering by the Selling Stockholders assuming all of the shares registered for resale hereby are sold.

The Selling Stockholders may sell some, all or none of their Resale Shares. We do not know how long the Selling Stockholders will hold the Resale Shares before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale or other disposition of any of the Resale Shares. The Resale Shares covered hereby may be offered from time to time by the Selling Stockholders, provided that (i) Resale Shares issued upon conversion of Series A Preferred Stock and Series B Preferred Stock may only be offered after such shares of Series A Preferred Stock and Series B Preferred Stock are converted to Common Stock pursuant to the terms of the Series A Certificate of Designation and Series B Certificate of Designation, respectively and (ii) Resale Shares issued upon exercise of Parapyre Warrants may only be offered after such Parapyre Warrants are exercised pursuant to the terms of the Parapyre Warrants.

The information set forth below is based upon information obtained from the Selling Stockholders and upon information in our possession regarding the issuance of the Resale Shares, and the Series A Preferred Stock, the Series B Preferred Stock and the Parapyre Warrants from which such Resales Sales are convertible or exercisable, as applicable, collectively in connection with the June 2023 Transactions, the December 2023 PIPE, the March 2024 PIPE and the April 2024 Exchange. The percentages of Common Stock owned after the offering by each Selling Stockholder below are based on 50,825,874 shares of Common Stock outstanding as of August 15, 2024, and, for each Selling Stockholder, assumes the conversion or exercise, as applicable, of only the Series A Preferred Stock, Series B Preferred Stock and Parapyre Warrants owned by such Selling Stockholder but not the Series A Preferred Stock, Series B Preferred Stock and Parapyre Warrants owned by any other Selling Stockholder. The numbers of shares of Common Stock beneficially owned before and after the offering presented in the table below do not give effect to any beneficial ownership limitations with respect to the Series A Preferred Stock, Series B Preferred Stock and Parapyre Warrants.

Name of Selling Stockholders ⁽¹⁾	Common Stock Beneficially Owned Before Offering ⁽²⁾	Common Stock that May Be Offered Pursuant to Prospectus	Common Stock Beneficially Owned After Offering ⁽²⁾	
			Number	Percentage (%)
Entities associated with Fairmount Funds Management LLC ⁽³⁾	18,526,581	18,526,581	—	*
Entities associated with RTW Investments, LP ⁽⁴⁾	3,258,360	3,258,360	—	*
Perceptive Life Sciences Master Fund, Ltd. ⁽⁵⁾	3,031,018	2,986,054	44,964	*
Entities associated with Venrock Healthcare Capital Partners ⁽⁶⁾	2,685,448	2,685,448	—	*
Braidwell Partners Master Fund LP ⁽⁷⁾	2,514,538	1,108,000	1,406,538	2.8
Parapyre Holding LLC ⁽⁸⁾	2,057,989	2,057,989	—	*
AI Biotechnology LLC ⁽⁹⁾	2,133,840	2,000,000	133,840	*
Commodore Capital Master LP ⁽¹⁰⁾	1,988,084	1,871,760	116,324	*
Fidelity Growth Company Commingled Pool ⁽¹¹⁾	1,399,314	460,763	938,551	1.8
Cameron Turtle ⁽¹²⁾	1,385,445	746,507	157,657	*
Paragon Therapeutics, Inc. ⁽¹³⁾	1,373,582	1,373,582	—	*
Avoro Life Sciences Fund LLC ⁽¹⁴⁾	1,122,000	1,122,000	—	*
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund ⁽¹¹⁾	1,049,980	366,184	683,796	1.3
Adage Capital Partners LP ⁽¹⁵⁾	1,014,477	150,743	950,734	1.9
Deep Track Capital, LP ⁽¹⁶⁾	1,000,000	1,000,000	—	*

Entities associated with Franklin Biotechnology ⁽¹⁷⁾	760,580	687,080	73,500	*
Boxer Capital, LLC ⁽¹⁸⁾	696,480	696,480	—	*
Entities associated with Driehaus Capital Management LLC ⁽¹⁹⁾	687,080	687,080	—	*
Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund ⁽¹¹⁾	629,468	455,168	174,300	*
Affinity Healthcare Fund, LP ⁽²⁰⁾	538,420	261,113	277,307	*
Polar Capital Funds Plc — Biotechnology Fund ⁽²¹⁾	500,000	233,320	266,680	*
Entities associated with Logos Global Master Fund LP ⁽²²⁾	450,000	450,000	—	*
Citadel CEMF Investments Ltd. ⁽²³⁾	412,240	412,240	—	*
Atlas Diversified Master Fund, Ltd. ⁽²⁴⁾	405,904	202,600	203,304	*
Entities advised or subadvised by T. Rowe Price Associates, Inc. ⁽²⁵⁾	405,400	405,400	—	*
Spyre Advisors LLC ⁽²⁶⁾	373,253	373,253	—	*
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company K6 Fund ⁽¹¹⁾	335,784	116,531	219,253	*
Walleye Opportunities Master Fund Ltd. ⁽²⁷⁾	314,906	67,600	247,306	*
Entities associated with Blackstone Alternative Asset Management Associates LLC ⁽²⁸⁾	292,995	276,739	16,256	*
CDK Associates, L.L.C. ⁽²⁹⁾	264,180	264,180	—	*
Fidelity Select Portfolios: Biotechnology Portfolio ⁽¹¹⁾	261,553	33,334	228,219	*
Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund ⁽¹¹⁾	254,704	98,104	156,600	*
Woodline Master Fund LP ⁽³⁰⁾	181,000	181,000	—	*
Andrew Spencer ⁽³¹⁾	170,576	91,387	79,189	*
Janet Gunzner-Toste ⁽³²⁾	169,100	91,387	77,713	*
Fidelity Select Portfolios: Pharmaceuticals Portfolio ⁽¹¹⁾	148,742	136,582	12,160	*
Quantum Partners LP ⁽³³⁾	145,000	67,600	77,400	*
Stempoint Capital Master Fund LP ⁽³⁴⁾	140,450	27,000	113,450	*
Justin LaFountaine ⁽³⁵⁾	126,201	74,650	51,551	*
Wedbush Healthcare Partners 2023 Fund, LLC ⁽³⁶⁾	68,720	68,720	—	*
Salthill Partners, L.P. ⁽³⁷⁾	50,075	50,075	—	*
Salthill Investors (Bermuda) L.P. ⁽³⁷⁾	43,185	43,185	—	*
Sessions LLC ⁽³⁸⁾	34,360	34,360	—	*
Third Street Holdings LLC ⁽³⁹⁾	16,900	16,900	—	*
Harry Turtle ⁽⁴⁰⁾	13,760	13,760	—	*

* Less than 1%

- (1) To our knowledge, unless otherwise indicated, all persons named in the table above have sole voting and investment power with respect to their shares of Common Stock. Unless an address is provided below, the address for the holder is 221 Crescent Street, Building 23, Suite 105, Waltham MA 02453.
- (2) “Beneficial ownership” is a term broadly defined by the SEC in Rule 13d-3 under the Exchange Act, and includes more than the typical form of stock ownership, that is, stock held in the person’s name. The term also includes what is referred to as “indirect ownership,” meaning ownership of shares as to which a person has or shares investment power. Notwithstanding the foregoing, the beneficial ownership amounts assume the sale of all Common Stock that may be offered pursuant to this prospectus without taking into account certain limitations, including that (A) a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of Common Stock (i) prior to the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred

- Stock, or (ii) if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.00% and 19.99%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion, (B) a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of Common Stock (i) prior to the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock, or (ii) if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.00% and 19.99%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion, and (C) a holder of Parapyre Warrants is prohibited from exercising such warrants if, as a result of such exercise, such holder, together with its affiliates, would beneficially own more than 4.99% of the total number of shares of Common Stock issued and outstanding immediately after giving effect to the issuance of shares of Common Stock issuable upon such exercise.
- (3) Consists of (i) 13,841,800 shares of Common Stock issuable upon the conversion of Series A Preferred Stock, (ii) 4,018,101 shares of Common Stock, and (iii) 666,680 shares of Common Stock issuable upon the conversion of Series B Preferred Stock all held by Fairmount Healthcare Fund II LP ("Fund II"). Fairmount Funds Management LLC ("Fairmount") serves as investment manager for Fund II and may be deemed a beneficial owner of any securities of the Company held by Fund II. Fund II has delegated to Fairmount the sole power to vote and the sole power to dispose of all securities held in Fund II's portfolio. Because Fund II has divested itself of voting and investment power over the securities it holds and may not revoke that delegation on less than 61 days' notice, Fund II disclaims beneficial ownership of the securities it holds. The general partner of Fairmount is Fairmount Funds Management GP LLC ("Fairmount GP"). As managing members of Fairmount GP, Peter Harwin and Tomas Kiselak may be deemed beneficial owners of any securities of the Company beneficially owned by Fairmount. Fairmount GP, Fairmount, Mr. Harwin and Mr. Kiselak disclaim beneficial ownership of securities held by Fund II, except to the extent of their pecuniary interest therein. The address for the beneficial owners is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA 19428. The shares of Common Stock issuable upon conversion of the shares of Series A Preferred Stock and Series B Preferred Stock held by Fund II is subject to a Beneficial Ownership Limitation of 9.99%.
 - (4) Consists of an aggregate of 3,258,360 shares of Common Stock held by RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Biotech Opportunities Operating Ltd. (collectively, the "RTW Funds"). RTW Investments, LP ("RTW"), in its capacity as the investment manager of the RTW Funds, has the power to vote and the power to direct the disposition of the shares held by the RTW Funds. Accordingly, RTW may be deemed to be the beneficial owner of such securities. Roderick Wong, M.D., as the Managing Partner of RTW, has the power to direct the vote and disposition of the securities held by RTW. Dr. Wong disclaims beneficial ownership of the shares held by the RTW Funds, except to the extent of his pecuniary interest therein. The address and principal office of RTW Investments, LP is 40 10th Avenue, Floor 7, New York, NY 10014, and the address of Dr. Wong and each of the RTW Funds is c/o RTW Investments, LP, 40 10th Avenue, Floor 7, New York, NY 10014.
 - (5) Consists of 3,031,018 shares of Common Stock held by Perceptive Life Sciences Master Fund, Ltd ("Perceptive Fund"). Perceptive Advisors LLC ("Perceptive Advisors") is the investment advisor of Perceptive Fund and may be deemed to have beneficial ownership of the shares beneficially owned thereby. Joseph Edelman is the controlling person of each of Perceptive Fund and Perceptive Advisors and, accordingly, may be deemed to have beneficial ownership of the shares beneficially owned by each of Perceptive Fund and Perceptive Advisors. Mr. Edelman disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of Perceptive is 51 Astor Place, 10th Floor, New York, NY 10003.
 - (6) Consists of (i) 2,328,026 shares of Common Stock held by Venrock Healthcare Capital Partners EG, L.P. ("VHCP EG"), (ii) 324,917 shares of Common Stock held by Venrock Healthcare Capital Partners III, L.P. ("VHCP III"), and (iii) 32,505 shares of Common Stock held by VHCP Co-Investment Holdings III, LLC ("VHCP III Co"). VHCP Management III, LLC ("VHCPM") is the sole general partner of VHCP III and the sole manager of VHCP III Co. VHCP Management EG, LLC ("VHCPM EG") is the sole general partner of VHCP EG. Dr. Bong Koh and Nimish Shah are the voting members of VHCPM and VHCPM EG. The address of each of these persons and entities is 7 Bryant Park, 23rd Floor, New York, NY 10018.
 - (7) Consists of 2,514,538 shares of Common Stock held by Braidwell Partners Master Fund LP ("Braidwell Partners"). Braidwell LP (the "Braidwell Investment Manager") is the investment manager of Braidwell Partners, Braidwell GP LLC (the "Braidwell GP") is the general partner of Braidwell Partners, and Braidwell Management LLC (the "Braidwell IM GP") is the general partner of the Braidwell Investment Manager and the managing member of the Braidwell GP. Messrs. Alexander T. Karnal and Brian J. Kreiter (together with Braidwell Partners, the Braidwell Investment Manager, the Braidwell GP and the Braidwell IM GP, the "Braidwell Parties") together own, directly or indirectly, the Braidwell Investment Manager, the Braidwell GP and the Braidwell IM GP. The address of Braidwell Partners is c/o Maples Corporate Services Limited, P.O Box 309, Ugland House, Grand Cayman, KY1-1104 Cayman Islands. The principal address of the Braidwell Investment Manager, the Braidwell GP and the Co-Founders is One Harbor Point, 2200 Atlantic Street, 4th Floor, Stamford, Connecticut 06902. The Braidwell Parties may be deemed to have shared voting and dispositive powers with respect to the shares of Common Stock held by Braidwell Partners. Each of the Braidwell Parties disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
 - (8) Consists of (i) 1,373,582 shares of Common Stock held by Parapyre and (ii) 684,407 shares of Common Stock issuable upon the exercise of warrants held by Parapyre. Parapyre is managed by K. Evan Thompson. The shares of Common Stock issuable upon the exercise of the Parapyre Warrants is subject to a Beneficial Ownership Limitation of 4.99%.
 - (9) Consists of 2,133,840 shares of Common Stock held by AI Biotechnology LLC. Access Industries Holdings LLC, or AIH, directly controls all of the outstanding voting interest in AI Biotechnology LLC. Access Industries Management, LLC, or AIM, controls AIH. Len Blavatnik controls AIM and holds a majority of the outstanding voting interests in AIH. Each of Len Blavatnik, AIM and AIH may be deemed to have voting and investment power over the shares held by AI Biotechnology LLC. The address of each of AI Biotechnology LLC, AIM, AIH and Len Blavatnik is c/o Access Industries, Inc. 40 West 57th Street, 28th Floor, New York, NY 10019.
 - (10) Consists of 1,988,084 shares of Common Stock held by Commodore Capital Master LP. Commodore Capital LP is the investment manager to Commodore Capital Master LP and may be deemed to beneficially own the shares held by Commodore Capital Master LP. Michael Kramarz and Robert Egen Atkinson are the managing partners of Commodore Capital LP and exercise investment discretion with respect to these shares. Commodore Capital LP and Commodore Capital Master LP have shared voting and dispositive power with respect to these shares. The address of Commodore Capital LP and Commodore Capital Master LP is 444 Madison Avenue, 35th Floor, New York, NY 10022.

- (11) These funds and accounts are managed by direct or indirect subsidiaries of FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. The address of these funds and accounts is 245 Summer Street, Boston, MA 02210.
- (12) Consists of (i) 747,940 shares of Common Stock and (ii) 637,505 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of August 15, 2024, held by Dr. Turtle.
- (13) Consists of 1,373,582 shares of Common Stock held by Paragon. Paragon is managed by a board of directors.
- (14) Consists of 1,122,000 shares of Common Stock held by Avoro Life Sciences Fund LLC. Avoro Capital Advisors LLC ("Avoro") is the investment advisor for Avoro Life Sciences Fund LLC. Behzad Aghazadeh serves as the portfolio manager and controlling person of Avoro and may be deemed to have investment discretion and voting power over the shares held by Avoro. Mr. Aghazadeh disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest in such shares, if any. The address of Avoro Life Sciences Fund LLC is 110 Greene Street, Suite 800, New York, NY 10012.
- (15) Consists of 1,014,477 shares of Common Stock held by Adage Capital Partners LP ("Adage"). Bob Atchinson and Phillip Gross are the managing members of Adage Capital Advisors, L.L.C., which is the managing member of Adage Capital Partners GP, L.L.C., which is the general partner of Adage, and each such person or entity, as the case may be, has shared voting and/or investment power over the securities held by Adage Capital Partners, LP and may be deemed the beneficial owner of such shares, and each such person or entity, as the case may be, disclaims beneficial ownership of such securities except to the extent of their respective pecuniary interest therein.
- (16) Consists of 1,000,000 shares of Common Stock held by Deep Track Biotechnology Master Fund, Ltd. ("Deep Track Biotech"). Deep Track Capital, LP ("Deep Track Capital") and David Kroin have shared voting power and shared dispositive power over the shares held by the Deep Track Biotech. Mr. Kroin may be considered a control person for Deep Track Capital. The address of Deep Track Capital and Mr. Kroin is 200 Greenwich Ave, 3rd Floor, Greenwich, CT 06830, and the address for Deep Track Biotech is 190 Elgin Avenue, George Town, KY1-9001, Cayman Islands.
- (17) Consists of (i) 273,800 shares of Common Stock held by Franklin Strategic Series – Franklin Biotechnology Discovery Fund ("Franklin Strategic") and (ii) 486,780 shares of Common Stock held by Franklin Templeton Investment Funds – Franklin Biotechnology Discovery Fund ("Franklin Templeton"). Franklin Advisers, Inc., a SEC registered broker-dealer, is the investment advisor to both Franklin Strategic and Franklin Templeton. Evan McCulloch is the portfolio manager for both Franklin Strategic and Franklin Templeton. Mr. McCulloch may be deemed to have voting and investment power over the common stock held by Franklin Strategic and Franklin Templeton. Mr. McCulloch disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of the Franklin entities is c/o Franklin Advisers, Inc., One Franklin Parkway, San Mateo, CA 94403.
- (18) Consists of 696,480 shares of Common Stock held by Boxer Capital, LLC ("Boxer Capital"). Boxer Asset Management Inc. ("Boxer Asset Management") is the managing member of Boxer Capital. Joseph C. Lewis, as the sole indirect owner of Boxer Asset Management, may be deemed to have shared power to vote (or direct vote) and/or to dispose (or direct the disposition) of the securities held by Boxer Capital. Boxer Asset Management and Joseph C. Lewis disclaim beneficial ownership over the shares owned by Boxer Capital except to the extent of their pecuniary interests therein. The principal address for Boxer Capital is 12860 El Camino Real, Ste 300, San Diego, CA 92130 and the principal address for Boxer Asset Management and Mr. Lewis is Cay House, EP Taylor Drive N7776, Lyford Cay, New Providence, Bahamas.
- (19) Consists of (i) 507,720 shares of Common Stock held by Driehaus Life Sciences Master Fund, L.P. ("Driehaus Master Fund") and (ii) 179,360 shares of Common Stock held by Driehaus Life Sciences (QP) Fund, L.P. ("Driehaus QP Fund"). Driehaus Capital Management (USVI) LLC is the general partner of both Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund, L.P. By virtue of such relationship, Driehaus Capital Management (USVI) LLC may be deemed to have beneficial ownership over such securities. Driehaus Capital Management LLC is the investment advisor to both Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund. Driehaus Capital Management LLC exercises voting and investment power through portfolio managers comprised of Michael Caldwell and Alex Munns, each of whom disclaims beneficial ownership of the shares held by Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund, L.P. The address for these entities is c/o Driehaus Capital Management LLC, 25 East Erie Street, Chicago, IL 60611.
- (20) Consists of 538,420 shares of Common Stock held by Affinity Healthcare Fund, LP (the "Affinity Fund"). Affinity Asset Advisors, LLC (the "Affinity Advisor") is the investment manager of Affinity Fund and exercises investment discretion with regard to the shares of Common Stock owned by Affinity Fund. Affinity Fund and Affinity Advisor have the shared power to vote or to direct the vote and to dispose or direct the disposition of such shares of Common Stock owned by Affinity Fund. Affinity Advisor may be deemed to be the beneficial owner of such shares of Common Stock owned by Affinity Fund by virtue of its position as investment manager of Affinity Fund. The address of each of these entities is 767 3rd Avenue, Floor 15, New York, NY 10017.
- (21) Consists of 500,000 shares of Common Stock held by Polar Capital Funds plc – Biotechnology Fund. Polar Capital Funds plc is a company with variable capital and segregated liability between sub-funds incorporated in Ireland and authorized by the Central Bank of Ireland pursuant to the European Communities (Undertakings for Investment in Transferable Securities) Regulations 2011, as amended and with the address George's Court, 54-62 Townsend Street, Dublin 2, Ireland. The investment manager of Polar Capital Funds plc is Polar Capital LLP, an FCA and SEC regulated fund manager/investment advisor, which has the ability to make decisions with respect to the voting and disposition of the shares and has overall responsibility for directing the investments of the entities in accordance with their investment objectives, policies and limitations. Polar Capital LLP is 100% owned by Polar Capital Partners Ltd, which is in turn 100% owned by Polar Capital Holdings plc, a London AIM listed holding company. Certain directors/employees are beneficial owners of Polar Capital Holdings plc but each such individual disclaims any beneficial ownership of the reported shares, other than to the extent they may or may not hold shares directly of the entities. The address for the investment manager is 16 Palace Street, London, United Kingdom, SW1E 5JD.
- (22) Consists of 450,000 shares of Common Stock held by Logos Global Master Fund LP ("Global Fund"). Logos GP LLC ("Logos GP") is the general partner of Global Fund. Logos Global Management LP ("Logos Global") is the investment advisor to Global Fund. Logos Global

- Management GP LLC (“Logos Global GP”) is the general partner of Logos Global. Arsani William and Graham Walmsley are the members of Logos GP and Mr. William is a control person of Logos Global and Logos Global GP. Mr. William and Mr. Walmsley each disclaim beneficial ownership of these shares, except to the extent of each’s pecuniary interest in such shares, if any. The principal address of Global Fund is 1 Letterman Drive, Building C, Suite C3-350, San Francisco, CA 94129.
- (23) Consists of 412,240 shares of Common Stock held by Citadel CEMF Investments Ltd. (“Citadel CEMF”). Citadel Advisors LLC (“Citadel Advisors”) is the portfolio manager of Citadel CEMF. Citadel Advisors Holdings LP (“Citadel Holdings”) is the sole member of Citadel Advisors. Citadel GP LLC (“Citadel GP”) is the General Partner of Citadel Holdings. Kenneth Griffin owns a controlling interest in Citadel GP LLC. Mr. Griffin, as the owner of a controlling interest in Citadel GP LLC, may be deemed to have shared power to vote and/or shared power to dispose of the securities held by Citadel CEMF. This disclosure shall not be construed as an admission that Mr. Griffin or any of the Citadel related entities listed above is the beneficial owner of any of the Company’s securities other than the securities actually owned by such person (if any). The address of Citadel CEMF is c/o Citadel Enterprise Americas LLC, Southeast Financial Center, 200 S. Biscayne Blvd., Suite 3300, Miami, FL 33131.
- (24) Consists of 405,904 shares of Common Stock held by Atlas Diversified Master Fund, Ltd. (“ADMF”). Balyasny Asset Management L.P. (“BAM”) is the investment manager of ADMF. Dmitry Balyasny indirectly controls the general partner of BAM and shall be deemed to have voting and investment control over the shares held by ADMF and may be deemed to beneficially own the shares beneficially owned by ADMF. The business address of ADMF is c/o Maples Corporate Services Limited, P.O. Box 309, Ugland House, George Town, Grand Cayman KY1-1104, Cayman Islands, and the business address of BAM and Dmitry Balyasny is 444 W. Lake Street, 50th Floor, Chicago, IL 60606.
- (25) Consists of (i) 386,880 shares of Common Stock held by T. Rowe Price Health Sciences Fund, Inc., (ii) 18,480 shares of Common Stock held by T. Rowe Price Health Sciences Portfolio, and (iii) 40 shares of Common Stock held by T. Rowe Price Multi-Strategy Total Return Fund, Inc. T. Rowe Price Associates, Inc. (“TRPA”), as investment adviser, has dispositive and voting power with respect to the shares held by these funds and accounts. For purposes of the Securities Exchange Act of 1934, TRPA may be deemed to be the beneficial owner of these aforementioned shares; however, TRPA expressly disclaims that it is, in fact, the beneficial owner of such securities. TRPA is a wholly owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The principal business address of TRPA is 100 East Pratt Street, Baltimore, MD 21202.
- (26) Consists of 373,253 shares of Common Stock held by Spyre Advisors LLC (“Spyre Advisors”). Spyre Advisors is managed by Damon Banks.
- (27) Consists of (i) 313,206 shares of Common Stock held by Walleye Opportunities Master Fund Ltd. (“Walleye Opportunities Fund”) and (ii) 1,700 shares of Common Stock held by Sea Hawk Multi-Strategy Master Fund Ltd. Walleye Opportunities Fund is a private investment fund managed by Walleye Capital LLC. William England is the chief executive officer of Walleye Capital LLC. As a result, Walleye Capital LLC and Mr. England may be deemed to have shared voting and dispositive power with respect to the securities held by Walleye Opportunities Fund. The business address of these entities is 2800 Lane N., Plymouth, MN 55447.
- (28) Consists of (i) 244,216 shares of Common Stock held by Blackstone Annex Master Fund L.P. (“Annex Fund”), (ii) 34,142 shares of Common Stock held by Spruce Street Aggregator L.P.–ECDF A1 (“ECDF A1”), and (iii) 14,637 shares of Common Stock held by Spruce Street Aggregator L.P.–ECDF A2 (“ECDF A2”, and together with ECDF A1, the “Aggregator Fund”). Blackstone Alternative Asset Management Associates LLC is the general partner of Annex Fund and the Aggregator Fund. Blackstone Holdings II L.P. is the sole member of Blackstone Alternative Asset Management Associates LLC. Blackstone Holdings I/II GP L.L.C. is the general partner of Blackstone Holdings II L.P. Blackstone Inc. is the sole member of Blackstone Holdings I/II GP L.L.C. Blackstone Group Management L.L.C. is the sole holder of the Series II preferred stock of Blackstone Inc. Blackstone Group Management L.L.C. is wholly owned by its senior managing directors and controlled by its founder, Stephen A. Schwarzman. Each of such Blackstone entities and Mr. Schwarzman may be deemed to beneficially own the securities beneficially owned by the Annex Fund and the Aggregator Fund directly or indirectly controlled by it or him, but each (other than each of the Annex Fund and the Aggregator Fund to the extent of their respective direct holdings) disclaims beneficial ownership of such securities. The address of each of the entities listed is c/o Blackstone Inc., 345 Park Avenue, New York, New York 10154.
- (29) Consists of 264,180 shares of Common Stock held by CDK Associates, L.L.C. (“CDK”). Bruce Kovner has voting and/or dispositive power over the holdings of CDK. The address of CDK is c/o CAM Capital 731 Alexander Road, Bldg 2, Suite 500, Princeton, NJ 08540.
- (30) Consists of 181,000 shares of Common Stock held by Woodline Master Fund LP (the “Woodline Fund”). Woodline Partners LP serves as the investment manager of Woodline Fund and may be deemed to be the beneficial owner of the shares. Woodline Partners LP disclaims any beneficial ownership of these shares. The address of this fund and account is 4 Embarcadero Center, Suite 34590, San Francisco, CA 94111.
- (31) Consists of (i) 92,863 shares of Common Stock and (ii) 77,713 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of August 15, 2024, held by Dr. Spencer.
- (32) Consists of (i) 91,387 shares of Common Stock and (ii) 77,713 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of August 15, 2024, held by Dr. Gunzner-Toste.
- (33) The shares listed herein are held for the account of Quantum Partners LP, a Cayman Islands exempted limited partnership (“Quantum Partners”). Soros Fund Management LLC (“SFM LLC”) serves as principal investment manager to Quantum Partners. As such, SFM LLC has been granted investment discretion over portfolio investments, including the shares, held for the account of Quantum Partners. George Soros serves as Chairman of SFM LLC and has sole discretion to replace FPR Manager LLC, the manager of SFM LLC. The address for Quantum Partners is c/o Soros Fund Management LLC, 250 West 55th Street, New York, NY 10019.
- (34) Consists of (i) 74,000 shares of Common Stock held by StemPoint Capital Master Fund LP (“StemPoint Fund”) and (ii) 66,450 shares of Common Stock held by Jefferies Strategic Investments, LLC (“JSI”). StemPoint Capital LP (“Stempoint”) serves as investment advisor to StemPoint Fund and JSI. StemPoint exercises voting and investment power over the shares held by each of StemPoint Fund and JSI pursuant to investment management agreements. StemPoint hereby disclaims beneficial ownership of the shares held by StemPoint Fund and JSI. The total number of shares that StemPoint exercises voting and investment power over is 140,450, as of August 15, 2024. The address of these funds and accounts is 520 Madison Avenue, 19th Floor, New York, NY 10022.
- (35) Consists of (i) 75,747 shares of Common Stock and (ii) 50,454 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of August 15, 2024, held by Mr. LaFountaine.

- (36) Consists of 68,720 shares of Common Stock held by Wedbush Healthcare Partners 2023 Fund, LLC. The address for Wedbush Healthcare Partners 2023 Fund, LLC is Wedbush Center, 1000 Wilshire Blvd., Los Angeles, CA 90017.
- (37) Consists of (i) 43,185 shares of Common Stock held by Salthill Investors (Bermuda) L.P. (“Salthill Investors”) and (ii) 50,075 shares of Common Stock held by Salthill Partners, L.P. (“Salthill Partners” and together with Salthill Investors, the “Wellington Selling Stockholders”). Wellington Management Company LLP (“WMC”) has the power to vote and dispose of the securities pursuant to WMC’s capacity as investment advisor on behalf of the Wellington Selling Stockholders. WMC is a subsidiary of Wellington Management Group LLP (“WMG”). WMG is a Massachusetts limited liability partnership, privately held by 204 partners (as of January 1, 2024). There are no external entities with any ownership interest in the firm. No single partner owns or has the right to vote more than 5% of WMC’s capital. Additional information about WMC is available in its Form ADV filed with the SEC. The address of the Wellington entities is 280 Congress Street, Boston, MA 02210.
- (38) Consists of 34,360 shares of Common Stock held by Sessions LLC. The address for Sessions LLC is 96 Fairbanks Ave, Wellesley, MA 02481.
- (39) Consists of 16,900 shares of Common Stock held by Third Street Holdings LLC (“Third Street”). Peter P. D’Angelo has voting and/or dispositive power over the holdings of Third Street Holdings, LLC. The address of Third Street is c/o CAM Capital 731 Alexander Road, Bldg 2, Suite 500, Princeton, NJ 08540.
- (40) Consists of 13,760 shares of Common Stock held by Harry Turtle.

Relationship with the Selling Stockholders

Cameron Turtle is our Chief Executive Officer, Andrew Spencer is our SVP, Preclinical R&D, Janet Gunzner-Toste is our SVP, Operations and Justin LaFountaine is our SVP, Corporate Development.

Wedbush PacGrow served as lead financial advisor to our board of directors with respect to the Asset Acquisition.

Paragon and Parapyre each beneficially owns less than 5% of our capital stock through their respective holdings of our common stock. Fairmount beneficially owns more than 5% of our capital stock, has two seats on our board of directors (the “Board”) and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount appointed Paragon’s board of directors and has the contractual right to approve the appointment of any executive officers. Parapyre is an entity formed by Paragon as a vehicle to hold equity in Pre-Merger Spyre in order to share profits with certain employees of Paragon.

In connection with the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement, pursuant to which we have exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights with respect to certain research programs, including with respect to our product candidates. Under the Paragon Agreement, we are obligated to compensate Paragon on a quarterly basis for its services performed under each research program based on the actual costs incurred with mark-up costs pursuant to the terms of the Paragon Agreement. Furthermore, we are obligated to provide certain equity grants to Parapyre upon the completion of each of the calendar years ending on December 31, 2023 and December 31, 2024 to purchase 1% of the then outstanding shares of our Common Stock, on a fully diluted basis, on the last business day of each applicable calendar year, at the fair market value determined by the Board. The Parapyre Warrants were issued in order to settle our 2023 obligation under the Paragon Agreement. Pursuant to the Paragon Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, we are required to pay Paragon a nonrefundable fee in cash of \$0.8 million. On July 12, 2023, December 14, 2023, and June 5, 2024, we exercised our option available under the Paragon Agreement with respect to the SPY001, SPY002, and SPY003 research programs, respectively, and we entered into the SPY001 License Agreement and the SPY002 License Agreement on May 14, 2024. We are negotiating a license agreement with respect to SPY003 as of the date of this prospectus. Our option available under the Paragon Agreement with respect to the SPY004 program remains unexercised. Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, we became obligated to pay Paragon up to \$22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones. With respect to the SPY002 License Agreement only, on a product by product basis, the Company will pay sublicensing fees of up to approximately \$20 million upon the achievement of mostly commercial milestones. With respect to the SPY003 research program and, subject to the execution of the option, with respect to the SPY004 research program, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs, respectively.

In connection with the June 2023 Transactions, we entered into the Acquisition Agreement and the June 2023 SPA with certain of the Selling Stockholders. We issued to Fairmount (i) 378,421 shares of Common Stock and 265,263 shares of Series A Preferred Stock in exchange for shares of Pre-Merger Spyre based on a fixed exchange ratio of 0.5494488 to 1 pursuant to the Acquisition Agreement and (ii) 257,661 shares of Series A Preferred Stock at a price of \$291.08 per share pursuant to the June 2023 SPA. In connection with the June 2023 PIPE, we also entered into the June 2023 RRA with certain of the Selling Stockholders, including Fairmount, pursuant to which the June 2023 Investors are entitled to certain resale registration rights with respect to shares of our Common Stock held by such investors.

In connection with the December 2023 PIPE, we entered into the December 2023 SPA with certain of the Selling Stockholders. Pursuant to the December 2023 SPA, we issued capital stock to certain of our affiliates or stockholders currently or then holding 5% or more of our common stock, including (i) 16,667 shares of Series B Preferred Stock to Fairmount, (ii) 1,666,666 shares of Common Stock to entities associated with FMR LLC, (iii) 710,000 shares of Common Stock and 18,083 shares of Series B Preferred Stock to Perceptive Life Sciences Master Fund, Ltd., (iv) 250,000 shares of Common Stock and 35,417 shares of Preferred Stock to entities associated with Venrock Healthcare Capital Partners, (v) 515,000 shares of Common Stock and 12,125 shares of Series B Preferred Stock to entities associated with RTW Investments, LP, (vi) 235,000 shares of Common Stock and 5,792 shares of Series B Preferred Stock to Deep Track Biotechnology Master Fund, Ltd., and (vii) 50,000 shares of Common Stock and 1,250 shares of Series B Preferred Stock to Commodore Capital Master LP, at a price of \$15.00 per share of Common Stock and \$600.00 per share of Series B Preferred Stock. In connection with the December 2023 PIPE, we also entered into the December 2023 RRA with certain of the Selling Stockholders, including the above-named investors, pursuant to which such Selling Stockholders are entitled to certain resale registration rights with respect to shares of our Common Stock held by such investors.

In connection with the March 2024 PIPE, we entered into the March 2024 SPA with certain of the Selling Stockholders. Pursuant to the March 2024 SPA, we issued capital stock to certain of our affiliates or stockholders currently or then holding 5% or more of our common stock, including (i) 6,755 shares of Series B Preferred Stock to Perceptive Life Sciences Master Fund, Ltd., (ii) 13,515 shares of Series B Preferred Stock to entities associated with RTW Investments, LP, and (iii) 1,350 shares of Series B Preferred Stock to Commodore Capital Master LP, at a price of \$1,480.00 per share of Series B Preferred Stock. In connection with the March 2024 PIPE, we also entered into the March 2024 RRA with certain of the Selling Stockholders, including the above-named investors, pursuant to which such Selling Stockholders are entitled to certain resale registration rights with respect to shares of our Common Stock held by such investors.

Pursuant to the terms of the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, respectively, we agreed to prepare and file with the SEC resale a registration statement to register the Registrable Securities (as defined in the respective registration rights agreement) and, subject to certain exceptions, use commercially reasonable efforts to keep the registration statement effective under the Securities Act for so long as such securities registered for resale thereunder retain their character as Registrable Securities. We also agreed, among other things, to indemnify the certain Selling Stockholders, and each of their respective officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents, each person who controls any such Selling Stockholder and the officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents of each such controlling person from certain liabilities and pay all fees and expenses (excluding any legal fees of the Selling Stockholder(s), and any underwriting discounts and selling commissions) incident to our obligations under the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, respectively.

On April 23, 2024, we entered into the April 2024 Exchange Agreement with Fairmount, pursuant to which Fairmount agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of Common Stock.

PLAN OF DISTRIBUTION

We are registering the Resale Shares issued to the Selling Stockholders to permit the sale, transfer or other disposition of these shares by the Selling Stockholders or their donees, pledgees, transferees or other successors-in-interest from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the Selling Stockholders of the Resale Shares. We will, or will procure to, bear all fees and expenses incident to our obligation to register the Resale Shares.

The Selling Stockholders may sell all or a portion of the Resale Shares beneficially owned by them and offered hereby from time to time, and in the case of the Resale Shares issuable upon the conversion or exercise, as applicable, of Series A Preferred Stock, Series B Preferred Stock and Parapyre Warrants, may only be offered after such shares or warrants are converted to Common Stock pursuant to the terms of the Series A Certificate of Designation and the Series B Certificate of Designation or exercised pursuant to the terms of the Parapyre Warrants, as applicable, directly or through one or more underwriters, broker-dealers or agents. If the Resale Shares are sold through underwriters or broker-dealers, the Selling Stockholders will be responsible for underwriting discounts (it being understood that the Selling Stockholders shall not be deemed to be underwriters solely as a result of their participation in this offering) or commissions or agent's commissions. The Resale Shares may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. The Selling Stockholders may use any one or more of the following methods when selling Resale Shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- to or through underwriters or purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the Selling Stockholders to sell a specified number of such shares at a stipulated price per share;
- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The Selling Stockholders also may resell all or a portion of the Resale Shares in open market transactions in reliance upon Rule 144, as permitted by that rule, or Section 4(a)(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the Selling Stockholders may arrange for other broker-dealers to participate in sales. If the Selling Stockholders effect such transactions by selling Resale Shares to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the Selling Stockholders or commissions from purchasers of the Resale Shares for

whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 2121; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2121.01.

In connection with sales of the Resale Shares or otherwise, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Resale Shares in the course of hedging in positions they assume. The Selling Stockholders may also sell Resale Shares short and if such short sale takes place after the date that this registration statement is declared effective by the SEC, the Selling Stockholders may deliver Resale Shares covered by this prospectus to close out short positions and to return borrowed Resale Shares in connection with such short sales. The Selling Stockholders may also loan or pledge Resale Shares to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the Selling Stockholders have been advised that they may not use Resale Shares the resale of which has been registered on this registration statement to cover short sales of our Common Stock made prior to the date the registration statement, of which this prospectus forms a part, has been declared effective by the SEC.

The Selling Stockholders may, from time to time, pledge or grant a security interest in some or all of the Resale Shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the Resale Shares from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus. The Selling Stockholders also may transfer and donate the Resale Shares in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The Selling Stockholders and any broker-dealer or agents participating in the distribution of the Resale Shares may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling Stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the applicable prospectus delivery requirements of the Securities Act including Rule 172 thereunder and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

Each Selling Stockholder has informed us that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the Resale Shares. Upon us being notified in writing by a Selling Stockholder that any material arrangement has been entered into with a broker-dealer for the sale of Common Stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such Selling Stockholder and of the participating broker-dealer(s), (ii) the number of Resale Shares involved, (iii) the price at which such the Resale Shares were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commissions and markups, which, in the aggregate, would exceed eight percent (8.0%).

Under the securities laws of some U.S. states, the Resale Shares may be sold in such states only through registered or licensed brokers or dealers. In addition, in some U.S. states the Resale Shares may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any Selling Stockholder will sell any or all of the Resale Shares registered pursuant to the shelf registration statement, of which this prospectus forms a part.

Each Selling Stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the Resale Shares by the Selling Stockholder and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the Resale Shares to engage in market-making activities with respect to the Resale Shares. All of the foregoing may affect the marketability of the Resale Shares and the ability of any person or entity to engage in market-making activities with respect to the Resale Shares.

We will pay all expenses of the registration of the Resale Shares pursuant to the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, including, without limitation, SEC filing fees and expenses of compliance with state securities or “blue sky” laws; provided, however, that each Selling Stockholder will pay all underwriting discounts and selling commissions, if any and any related legal expenses incurred by it. We will indemnify the Selling Stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, or the Selling Stockholders will be entitled to contribution. We may be indemnified by the Selling Stockholders against certain civil liabilities set forth in the June 2023 RRA, the December 2023 RRA or the March 2024 RRA, as applicable, including liabilities under the Securities Act, that may arise from any written information furnished to us by the Selling Stockholders specifically for use in this prospectus, in accordance with the related registration rights agreements, or we may be entitled to contribution.

LEGAL MATTERS

Certain legal matters relating to the validity of the Resale Shares offered by this prospectus will be passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2023 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The audited Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc. included in Exhibit 99.1 of Aeglea BioTherapeutics, Inc.'s Current Report on Form 8-K dated October 6, 2023 have been so incorporated in reliance on the report (which contains an emphasis of matter relating to the basis of presentation as described in Note 1 and contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statement) of PricewaterhouseCoopers LLP, independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC, and we have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered by this prospectus. This prospectus, which forms part of the registration statement, does not contain all of the information included in the registration statement, including its exhibits and schedules. For further information about us and the securities described in this prospectus, you should refer to the registration statement, its exhibits and schedules and our reports, proxies, information statements and other information filed with the SEC.

Our filings are available to the public on the Internet, through a database maintained by the SEC at www.sec.gov. We also maintain a website at www.spyre.com. We have included our website address for the information of prospective investors and do not intend it to be an active link to our website. Information contained on our website does not constitute a part of this prospectus or any applicable prospectus supplement (or any document incorporated by reference herein or therein).

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below (in each case, other than portions of documents not deemed to be filed):

- Annual Report on [Form 10-K](#) for the year ended December 31, 2023 filed with the SEC on February 29, 2024, as amended by the Amendment No. 1 on [Form 10-K/A](#) filed with the SEC on March 1, 2024 (and any portions of our [Definitive Proxy Statement on Schedule 14A](#) filed on April 1, 2024 that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2023);
- Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2024](#) and [June 30, 2024](#), filed with the SEC on May 9, 2024 and August 7, 2024, respectively;
- Current Reports on Form 8-K filed with the SEC on [October 6, 2023](#) (Items 8.01 and 9.01 only), [January 18, 2024](#), [February 5, 2024](#), [March 18, 2024](#), [April 25, 2024](#) and [May 15, 2024](#); and
- the description of our Common Stock contained in our registration statement on [Form 8-A](#) filed with the SEC on March 28, 2016, including any amendments or reports filed for the purpose of updating such description.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus incorporates by reference the documents listed above and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed, except that we are not incorporating by reference any information furnished (and not filed) with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K (unless expressly provided to the contrary).

You may request a copy of these filings (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein), at no cost, by contacting us, either orally or in writing, at the following:

Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, Massachusetts 02453
(617) 651-5940

Information about us is also available at our website at <http://www.spyre.com>. You may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. However, the information on our website is not a part of this prospectus and is not incorporated by reference into this prospectus. We have authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.

PART II
INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an estimate of the fees and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the issuance and distribution of the securities being registered. All amounts shown are estimates, except for the SEC registration fee.

	Amount
SEC registration fee	\$ 194,211
Legal fees and expenses	\$ 25,000
Accounting fees and expenses	\$ 25,000
Miscellaneous fees and expenses	\$ 5,789
Total	\$ 250,000

We will bear all costs, expenses and fees in connection with the registration of the shares of common stock registered hereby, including with regard to compliance with state securities or “blue sky” laws. The Selling Shareholders, however, will bear all underwriting commissions and discounts, if any, attributable to their sale of shares of common stock. All amounts are estimates except the SEC registration fee.

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law (the “DGCL”) authorizes a court to award, or a corporation’s board of directors to grant, indemnity to directors and officers under certain circumstances and subject to certain limitations. The terms of Section 145 of the DGCL are sufficiently broad to permit indemnification under certain circumstances for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

As permitted by the DGCL, the Company’s second amended and restated certificate of incorporation (as amended from time to time, our “Certificate of Incorporation”) contains provisions that eliminate the personal liability of its directors and officers for monetary damages for any breach of fiduciary duties as a director or officer, except liability for the following:

- any breach of the director’s or officer’s duty of loyalty to the Company or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- under Section 174 of the DGCL (regarding unlawful dividends and stock purchases); or
- any transaction from which the director or officer derived an improper personal benefit.

As permitted by the DGCL, the Company’s amended and restated bylaws (as amended from time to time, our “Bylaws”) provide that:

- the Company is required to indemnify its directors and executive officers to the fullest extent permitted by the DGCL, subject to very limited exceptions;
- the Company may indemnify its other employees and agents as set forth in the DGCL;
- the Company is required to advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by the DGCL, subject to very limited exceptions; and
- the rights conferred in the Bylaws are not exclusive.

The Company has entered, and intends to continue to enter, into separate indemnification agreements with its directors and executive officers to provide these directors and executive officers additional contractual assurances regarding the scope of the indemnification set forth in the Company's Certificate of Incorporation and Bylaws and to provide additional procedural protections. At present, there is no pending litigation or proceeding involving a director or executive officer of the Company regarding which indemnification is sought.

The indemnification provisions in the Company's Certificate of Incorporation, Bylaws and the indemnification agreements entered into or to be entered into between the Company and each of its directors and executive officers may be sufficiently broad to permit indemnification of the Company's directors and executive officers for liabilities arising under the Securities Act.

The Company currently carries liability insurance for its directors and officers. Two of the Company's directors, Peter Harwin and Tomas Kiselak, are also indemnified by their employer with regard to their service on the Company's board of directors.

Item 16. Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Exhibit No.	Description
2.1	<u>Agreement and Plan of Merger, dated June 22, 2023, by and among Aeglea BioTherapeutics, Inc. Aspen Merger Sub I, Inc., Sequoia Merger Sub II, LLC and Spyre Therapeutics, Inc. (incorporated by reference to Exhibit 2.1 to the Company's registration statement on Form S-1 filed on December 22, 2023).</u>
3.1	<u>Second Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.2 to the Company's Current Report Form 8-K filed on May 15, 2024).</u>
3.2	<u>Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on February 5, 2024).</u>
3.3	<u>Certificate of Designation of Series A Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.3 to the Company's registration statement on Form S-1 filed with the SEC on December 22, 2023).</u>
3.4	<u>Certificate of Designation of Series B Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.4 to the Company's registration statement on Form S-1 filed with the SEC on December 22, 2023).</u>
3.5	<u>Certificate of Amendment to Certificate of Designation of Series B Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on March 18, 2024).</u>
4.1	<u>Form of Common Stock Certificate (incorporated by reference to Exhibit 4.2 to the Company's registration statement on Form S-1 filed with the SEC on December 22, 2023).</u>
5.1	<u>Opinion of Gibson, Dunn & Crutcher LLP.</u>
23.1	<u>Consent of PricewaterhouseCoopers LLP.</u>
23.2	<u>Consent of PricewaterhouseCoopers LLP.</u>
23.3	<u>Consent of Gibson, Dunn & Crutcher LLP (included in Exhibit 5.1 hereto).</u>
24.1	<u>Power of Attorney (included on the signature pages to the registration statement).</u>
107	<u>Filing Fee Table.</u>

Item 17. Undertakings

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Filing Fee Table" filed as an exhibit in the effective registration statement; and
 - (iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i), (1)(ii), and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or

prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

- (5) That, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (6) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, Commonwealth of Massachusetts, on September 20, 2024.

Spyre Therapeutics, Inc.

By: /s/ Cameron Turtle, DPhil
Name: Cameron Turtle, DPhil
Title: *Chief Executive Officer*

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dr. Cameron Turtle and Mr. Scott Burrows, and each of them, as true and lawful attorneys-in-fact and agents, with full powers of substitution and resubstitution, for them and in their name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the SEC, and generally to do all such things in their names and behalf in their capacities as officers and directors to enable the Company to comply with the provisions of the Securities Act and all requirements of the SEC, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed below by the following persons in the capacities and on the dates indicated.

Signatures	Title	Date
<u>/s/ Cameron Turtle, DPhil</u> Cameron Turtle, DPhil	Chief Executive Officer & Director (<i>Principal Executive Officer</i>)	September 20, 2024
<u>/s/ Scott Burrows</u> Scott Burrows	Chief Financial Officer (<i>Principal Financial Officer and Principal Accounting Officer</i>)	September 20, 2024
<u>/s/ Jeffrey W. Albers</u> Jeffrey W. Albers	Chairman of the Board	September 20, 2024
<u>/s/ Peter Harwin</u> Peter Harwin	Director	September 20, 2024
<u>/s/ Michael Henderson, M.D.</u> Michael Henderson, M.D.	Director	September 20, 2024
<u>/s/ Tomas Kiselak</u> Tomas Kiselak	Director	September 20, 2024
<u>/s/ Mark McKenna</u> Mark McKenna	Director	September 20, 2024
<u>/s/ Sandra Milligan</u> Sandra Milligan	Director	September 20, 2024
<u>/s/ Laurie Stelzer</u> Laurie Stelzer	Director	September 20, 2024

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Spyre Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common stock, \$0.0001 par value per share ⁽¹⁾	Rule 457(c)	46,330,799 ⁽²⁾	\$28.40 ⁽³⁾	\$1,315,794,691.60 ⁽³⁾	0.00014760	\$194,211.30				
Carry Forward Securities												
Carry Forward Securities	N/A	N/A	N/A	N/A		N/A			N/A	N/A	N/A	N/A
	Total Offering Amounts					\$1,315,794,691.60		\$194,211.30				
	Total Fees Previously Paid							N/A				
	Total Fee Offsets							N/A				
	Net Fee Due							\$194,211.30				

- (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the “Securities Act”), this registration statement also covers such an indeterminate amount of shares of common stock as may become issuable to prevent dilution resulting from stock splits, stock dividends and similar events.
- (2) The amount registered consists of up to (i) 31,137,912 shares of Common Stock, (ii) 13,841,800 shares of Common Stock issuable upon the conversion of 346,045 shares of Series A Preferred Stock, (iii) 666,680 shares of Common Stock issuable upon the conversion of 16,667 shares of Series B Preferred Stock, and (iv) 684,407 shares of Common Stock issuable upon exercise of warrants to purchase Common Stock.
- (3) Estimated solely for the purpose of calculating the registration fee, based on the average of the high and low prices of the shares of Common Stock on The Nasdaq Global Select Market on September 16, 2024 (such date being within five business days of the date that this registration statement was first filed with the Securities and Exchange Commission, in accordance with Rule 457(c) under the Securities Act).

September 20, 2024

Spyre Therapeutics, Inc.
221 Crescent St. Building 23, Suite 105
Waltham, MA 02453

Re: Spyre Therapeutics, Inc.
Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Spyre Therapeutics, Inc., a Delaware corporation (the “Company”), in connection with the preparation and filing with the Securities and Exchange Commission (the “Commission”) of a Registration Statement on Form S-3 (the “Registration Statement”) pursuant to the Securities Act of 1933, as amended (the “Securities Act”), relating to the resale from time to time by the selling stockholders named therein of up to (i) 31,137,912 shares (the “Common Shares”) of the Company’s common stock, par value \$0.0001 per share (“Common Stock”), (ii) 13,841,800 shares (the “Series A Conversion Shares”) of Common Stock issuable upon the conversion of 346,045 shares of our Series A Non-Voting Convertible Preferred Stock, par value \$0.0001 per share (the “Series A Preferred Stock”), (iii) 666,680 shares (the “Series B Conversion Shares” and together with the Series A Conversion Shares, the “Conversion Shares”) of Common Stock issuable upon the conversion of 16,667 shares of Series B Non-Voting Convertible Preferred Stock, par value \$0.0001 (the “Series B Preferred Stock” and together with the Series A Preferred Stock, the “Preferred Stock”), and (iv) 684,407 shares (the “Warrant Shares”) of Common Stock issuable upon the exercise of 684,407 warrants (the “Warrants”).

In arriving at the opinion expressed below, we have examined originals, or copies certified or otherwise identified to our satisfaction as being true and complete copies of the originals, of the specimen common stock certificates and such other documents, corporate records, certificates of officers of the Company and of public officials and other instruments as we have deemed necessary or advisable to enable us to render these opinions. In our examination, we have assumed the genuineness of all signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals and the conformity to original documents of all documents submitted to us as copies.

Based on the foregoing, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that the Common Shares are validly issued, fully paid and non-assessable and the Conversion Shares, when issued upon the conversion of the Preferred Stock, and the Warrant Shares, when issued upon the exercise of the Warrants, will be validly issued, fully paid and non-assessable.

We consent to the filing of this opinion as an exhibit to the Registration Statement, and we further consent to the use of our name under the caption “Legal Matters” in the Registration Statement and the prospectus that forms a part thereof. In giving these consents, we do not thereby admit that we are within the

category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

/s/ Gibson, Dunn & Crutcher LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Spyre Therapeutics, Inc. of our report dated February 29, 2024, relating to the financial statements, which appears in Spyre Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2023. We also consent to the reference to us under the heading “Experts” in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Austin, Texas
September 20, 2024

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Spyre Therapeutics, Inc. of our report dated October 6, 2023, relating to the Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc., which appears in Spyre Therapeutics, Inc.'s Current Report on Form 8-K dated October 6, 2023. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Austin, Texas September 20, 2024